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Acute aluminum encephalopathy in a dialysis center caused by a cement mortar water distribution pipe

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Acute aluminum encephalopathy in a dialysis center caused by a cement mortar water distribution pipe.

Background. In Curaçao, distilled seawater from the water plant was used without further purification for hemodialysis for several decades. A new distribution pipe supplying water to a dialysis center on the island was installed in May 1996. To protect it from corrosion, this pipe was lined on the inside with a cement mortar. Because of the aggressiveness of the distilled water, calcium and aluminum (Al) leached from the cement mortar into the water used to prepare dialysate. This caused a possible hard water syndrome and definite acute Al intoxication.

Methods. We reviewed clinical details and outcome at follow-up, and arranged laboratory and toxicological studies of serum and hemodialysis water.

Results. Of the 27 patients who had a similar exposure (~60 hours) to the contaminated dialysate, 10 died from acute Al encephalopathy, whereas 17 patients had no or only minor symptoms and survived. The nonsurvivors were older (64 ± 3 years vs. 52 ± 2 years, $P < 0.01$) and had a lower body weight (57.5 ± 5.9 kg vs. 86.5 ± 4.1 kg, $P < 0.01$) and lower serum albumin concentrations (33 ± 1 vs. 36 ± 1 g/L, $P < 0.01$). Anuria tended to be more common in the nonsurvivors (8 out of 10 vs. 8 out of 17, $P > 0.05$). Serum Al concentrations, available in seven nonsurvivors, were significantly higher than in the survivors (808 ± 127 vs. 255 ± 25 μg/L, $P < 0.01$).

Conclusions. The water distribution pipe was lined with a cement mortar that was probably inappropriate for transporting drinking water. Water distribution facilities as well as the dialysis community should be aware of the possibility of Al leaching from cemented water distribution pipes. Similar Al loads appear to induce a more severe intoxication in malnourished, older patients with smaller Al distribution volumes and anuria.

Hemodialysis patients are very susceptible to changes in the composition of water used to produce dialysate. Their blood is brought in close contact with hundreds of liters of dialysate every week, and contaminants present in the water may diffuse across the dialysis membrane and cause intoxications. Therefore, guidelines for the composition of water used to generate dialysate are very strict [1, 2]. To reach this standard, most dialysis centers use more or less elaborate water purification systems, consisting of combinations of water softeners, activated carbon filters, deionizers, and reverse osmosis (RO) [3–6].

We report the combination of an acute aluminum (Al) intoxication and a possible hard water syndrome in a small dialysis unit on the island of Curaçao that traditionally used untreated tap water for dialysate production. The intoxication was caused by a newly installed drinking water conduit pipe leading to the dialysis center. This ductile iron pipe had an inner cement mortar lining from which Al and calcium (Ca) leached into the water used to prepare the dialysate. Although the patients had a similar exposure time to the contaminated dialysate, 10 patients became critically ill and died, whereas 17 had no or relatively mild symptoms and survived. A subgroup analysis was performed in an attempt to explain these interindividual differences.

METHODS

Dialysis center and water supply

Curaçao is a small island with 160,000 inhabitants. Approximately 90% of the population is of Afro-Caribbean origin. The prevalence of end-stage renal disease is 800 per million, which is among the highest in the world. Because of the large number of patients, a separate dialysis unit (Diatel Curaçao) with eight stations was opened in 1992 in addition to the hospital dialysis facility. On Curaçao, drinking water is produced by distillation of seawater. This expensive water treatment system produces very pure water (low ionic content, Al < 5 μg/L, Ca < 5 mg/L), which is of even better quality than produced by RO [6]. Before distribution, however, Ca and fluoride are added to the water supply in a low concentration. On Curaçao, as well as on other small Antillean

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islands, the municipal water supply has been used for more than two decades for dialysis without further purification. Because the local hospital intended to begin a high-flux dialysis program, for which ultrapure water is needed, an RO unit was installed in this institution in 1993. Because Diatel did not have a water storage tank and occasionally had insufficient water pressure for dialysis, installation of a spare water tank together with a RO unit for sterilization of the water was scheduled for August 1996. To solve the water pressure problem, the Water Company replaced a distribution pipe to the area of the center over a length of 2200 m. Water supply through this pipe started on May 21, 1996, after flushing the entire pipe. This cast iron pipe had an inner cement mortar lining to protect it from corrosion. The hospital received water supply via a different conduit pipe than Diatel.

At the time of replacement of the new conduit pipe, 29 patients were dialyzed in the dialysis unit. Patients were dialyzed three times per week during 3.5 to 4.5 hours using hollow fiber kidneys (Fresenius®, F6 and F8) and Braun® or Fresenius® dialysis machines. Untreated tap water was used to manufacture dialysate after passage through three particulate filters (25, 10, and 5 μm, respectively). The intended Ca content of the dialysate was 1.75 mmol/L. Because none of the patients used Al-containing phosphate binders and the Al content of tap water on Curaçao has traditionally been low, no regular serum Al determinations were made.

Epidemiology

The epidemiology of the intoxication on Curaçao was retrospectively analyzed by systematically reviewing dialysis and hospital charts and relevant laboratory sheets and correspondence. The day on which the new water distribution pipe was put into use (May 21, 1996) was designated "day 0" of the intoxication; all subsequent events, shown in Figure 1, were related to this starting date.

Serum aluminum: Sampling and assay

In 6 of the 10 patients who died (Table 1, patients 3 through 5 and 7 through 9), serum samples taken during admission in the third week of July 1996 (week 9 of the intoxication) were stored in the freezer in regular glass tubes. Samples of three healthy control subjects were obtained in the same tubes and processed in the same way as these patient samples. In three patients, no serum samples had been stored (patients 1, 2, and 6). In one patient (patient 10), who also eventually died, a serum sample for Al determination was obtained while he was still alive. This was done using the appropriate tubes mentioned later in this article. This was also the case for all the samples of the survivors obtained in the fourth week of July 1996 (week 10 of the intoxication). In these patients, serum samples were collected using Al-free polypropylene and polystyrene tubes prerinsed with 1 N HNO_3 to avoid Al contamination. All samples were sent by express mail to the Toxicology Laboratory (Leiden University Medical Center, Leiden, The Netherlands). The Al levels were analyzed with an atomic absorption spectrometer (Perkin Elmer 3030; Perkin Elmer, Norwalk, CT, USA) with a transversal Zeeman background correction system, using a graphite furnace (HGA 600) and pyrolytically coated graphite tubes. A calibration range was used between 0 and 200 μg/L (within-day precision was 13.8 and 6.1%, between-day precision was 22 and 8% for standard solutions 20 and 100 μg/L, respectively). For levels >200 μg/L, the calibration range was adapted between 200 and 1000 μg/L [7].

Other analytical methods

Intact parathyroid hormone (PTH) concentrations were measured by radio immunoassay (Elisa-PTH; Cis-Bio Int., Gif-sur-Yvette, France). Concentrations of Ca, alkaline phosphatase, ferritin, albumin, and mean cellular erythrocyte volume (MCV) were measured by standard laboratory methods.

Subgroup analysis

Two surviving patients with low serum Al levels (<60 μg/L) caused by a very short duration of exposure to the contaminated dialysate were excluded from this analysis. The remaining 27 patients were divided in two groups: survivors ($N = 17$) and nonsurvivors ($N = 10$). Both groups were compared with respect to the following characteristics: age, sex, body weight, presence of diabetes mellitus, diuresis, duration of exposure to contaminated dialysate, PTH status, severity of hypercalcemia, and initial serum Al concentration.

Statistical analysis

Data are expressed as mean ± SEM. The statistical significance of differences between mean values in the two groups was tested by Student's *t*-test for unpaired samples or the Mann–Whitney ranks sum test when appropriate. Fisher's exact test was used to test the difference of two proportions. Differences were considered to be of statistical significance at a P value of <0.05.

RESULTS

Epidemiology

The first day with regular dialysis sessions using water delivered through the new distribution pipe (May 21, 1996, day 0) was uneventful, but on the second and third days, several dialysis machines had transient conductivity alarms, possibly because of small air bubbles in the water mains. Extra flushing of the tap water solved this problem. The conductivity of the dialysate, measured by an

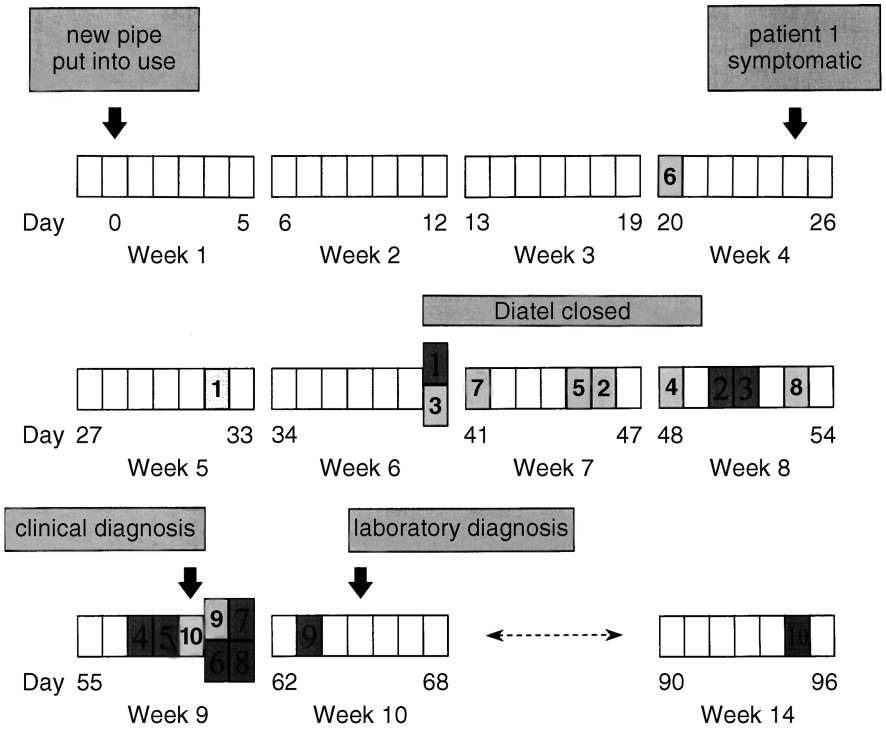

Fig. 1. Emergence of the acute aluminum (Al) intoxication. Day "0" (May 21, 1996) is the first day on which water was delivered to Diatel Curaçao through the new cemented water distribution pipe. On day "5" of week 9, the clinical diagnosis of "acute Al intoxication" was made, and on day "4" of week 10, this diagnosis was confirmed by a serum Al assay. Symbols are: (□) admission; (■) death; N = patient number.

external conductivity meter, was normal. The first patient (patient 6) was admitted to the hospital for a bleeding duodenal ulcer on June 10, 1996 (day 20; Fig. 1). On admission, she was slightly disoriented and developed seizures three weeks later (day 43) from which she died six weeks after admission (day 60). She may have been the first patient to become symptomatic because of Al intoxication, but it is also possible that she died of uremic encephalopathy with convulsions because dialysis was stopped two weeks prior to her death, and she had the shortest exposure time to the contaminated dialysate of all patients dying during the intoxication. The first patient (patient 1) without apparent underlying disease became symptomatic (myoclonus of jaw musculature) on June 15, 1996 (day 25). She was admitted to the hospital on June 22, 1996, because of hypercalcemia, nausea, vomiting, and confusion. She developed unexplained seizures and died on June 30, 1996 (day 40). On June 19, 1996 (day 29), seven patients had minor complaints of nausea and vomiting. Postdialysis hypercalcemia was observed in 25 of the 28 patients. The diagnosis "hard water syndrome" was made, and the use of Ca carbonate and vitamin D preparations was stopped. There was initial amelioration of the symptoms, but as the improvement was incomplete, the dialysis unit was closed on June 30, 1996 (day 40). All patients were referred to the hospital for dialysis where the symptoms of nausea, vomiting, as well as the hypercalcemia disappeared after a single dialysis with low Ca dialysate (1.50 mmol/L). From week 7 onward, transfusion-dependent microcytic anemia became evident (lowest MCV value: 70 ± 2 fL, N = 16). After installation of a RO system, including a deionizer, dialysis was resumed at the Diatel unit on July 10, 1996.

Unexpectedly, another eight patients (patients 2 through 5 and 7 through 10) had to be admitted to the hospital because of severe neurological symptoms (disorientation, myoclonus, convulsions and coma, N = 7) or unexplained sepsis (N = 2) with a delay of days to three weeks after the last dialysis with contaminated water (Fig. 1). Attempts to treat myoclonic jerks or seizures with intravenous diphantoin or diazepam were unsuccessful. The clinical diagnosis of acute Al intoxication was made on July 19, 1996 (day 59). Some days prior to this, the local toxicology laboratory reported a very high serum Al level in one patient using a semiquantitative method. Because the blood sample had not been processed correctly, the validity of this report was doubted initially, and blood samples were sent to the toxicology laboratory. When the diagnosis of "acute Al intoxication" was established by the results from this laboratory, on July 25, 1996 (day 65), nine patients had died (Fig. 1). A 10th patient, who was comatose, was transferred to a hospital in Florida (Florida Hospital, Orlando, FL, USA). Daily high-flux dialysis treatment combined with desferrioxamine administration was unsuccessful, and he died on August 24, 1996 (day 95). Seventeen patients who had elevated serum Al concentrations but were

Table 1. Characteristics of nonsurvivors and survivors

Patient number	Age *years*	Serum [Al][b] *μg/mL*	Sex	Weight *kg*	Exposure *hours*	Diuresis *mL/day*	PTH *pg/mL*	Albumin *g/L*
Nonsurvivors ($N = 10$)								
1	61	—	f	66	52	0	28	35
2	79	—	f	33	51	0	105	32
3	54	1189	m	85.5	68	150	52	34
4	64	725	f	52.5	52	0	22	35
5[a]	51	894	f	40	68	0	72	30
6	69	—	f	39.5	39	2000	—	28
7[a]	62	1275	m	62	60	0	8	34
8[a]	63	359	f	47	68	0	325	36
9[a]	74	517	f	86	64	0	32	32
10	65	696	m	64	68	0	480	35
Mean	64	808	—	57.5	59	—	125	33
SEM	3	127	—	5.9	3	—	55	1
Survivors ($N = 17$)								
11	64	490	m	57	68	0	710	40
12	57	395	m	65	59.5	0	80	39
13	50	321	f	87	68	0	21	34
14	44	319	m	97	62	0	630	39
15	49	318	m	57	66	200	50	36
16	23	315	f	104	68	0	97	39
17	66	303	f	78.5	64	60	280	34
18	57	301	f	90	68	350	170	37
19	50	248	f	57.5	64	1000	65	36
20	56	207	f	103	68	0	82	36
21	50	205	m	104	60	2	700	37
22	57	187	f	101	64	50	1200	32
23	57	182	f	95	62.5	1100	100	30
24	41	166	m	91.5	68	0	3	—
25	60	132	m	97.5	67	1200	270	39
26	41	116	m	93.2	60	200	680	38
27	56	113	f	91.5	67	1400	99	33
Mean	52[c]	255[c]	—	86.5[c]	65	—	308	36[d]
SEM	2	25	—	4.1	1	—	84	1

[a] Patients in whom post-mortem examination was performed
[b] Serum [Al], serum aluminum concentration
[c] $P < 0.01$, [d] $P < 0.05$, survivors vs. nonsurvivors

clinically asymptomatic were treated with intravenous desferrioxamine and high-flux dialysis according to the protocol suggested by Barata et al [8]. For logistical reasons, especially the inability to provide high-flux dialysis to all patients on short notice, these patients were transferred to six different hospitals in the Netherlands. Two patients, who in retrospect had been exposed to contaminated dialysate only briefly, did not need further treatment.

Calcium and aluminum content of tap water

Water supplied through the new pipe was first used for dialysis on May 21, 1996. On June 20, 1996 (day 30), the Ca-carbonate concentration of tap water delivered to the dialysis unit was 43 mg/L (17.2 mg/L or 0.45 mmol/L as Ca^{2+}), which is above the standard of 2 mg/L advised by the Association for the Advancement of Medical Instrumentation [2]. In the past, the Ca-carbonate concentration had been 15 to 20 mg/L (6.0 to 8.0 mg/L or 0.16 to 0.21 mmol/L Ca^{2+}). A sample of tap water obtained on July 3, 1996 (day 43), after the closing of Diatel was sent for analysis to Spectra Laboratories (Fremont, CA, USA). The results became available in August 1996. The Al content was excessively high (650 μg/L, normal below 10 μg/L), and the Ca^{2+} concentration was moderately elevated (18.1 mg/L, 0.47 mmol/L).

Serum calcium concentrations

In the two months prior to the intoxication, the mean predialysis total Ca concentration was 2.59 ± 0.05 mmol/L (April 1996) and 2.68 ± 0.05 mmol/L (May 1996). On two occasions in June 1996, when a hard water syndrome was suspected, Ca concentrations were determined before and after dialysis. The mean predialysis and postdialysis Ca concentrations were 2.75 ± 0.06 and 3.25 ± 0.06 mmol/L, respectively. The interdialytic drop was to 2.84 ± 0.05 mmol/L, with an increase to 3.27 ± 0.06 mmol/L after the next dialysis. The mean serum Ca concentrations in the survivors and nonsurvivors did not differ (Fig. 2).

Serum aluminum concentrations

The serum Al concentrations obtained in seven of the nonsurvivors were invariably very high (mean 808 ± 127

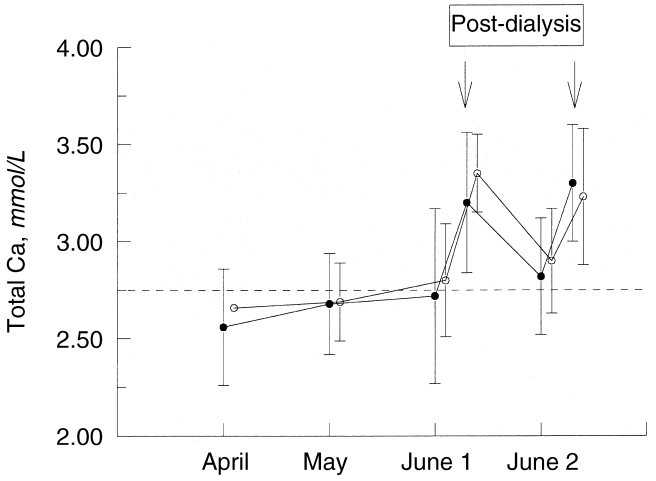

Fig. 2. Total serum Ca concentration in survivors (●) and nonsurvivors (○) of the Al intoxication. Data are presented as mean ± SEM. Postdialysis Ca concentrations were not available at the time of routine sampling in April and May. In June, samples were obtained both before and after two subsequent dialysis sessions taking place in weeks 5 and 6. The dotted line indicates the upper level of the normal range for our laboratory.

μg/L, range 359 to 1189 μg/L; Table 1). Seventeen of the surviving patients had clearly elevated serum Al concentrations (mean 255 ± 25 μg/L, range 113 to 490 μg/L). The average value obtained approximately one week later, when the surviving patients had been transferred to the Netherlands, was virtually the same as before the initiation of desferrioxamine treatment (248 ± 20 μg/L, $P > 0.05$). One patient, who had been exposed only briefly (5 hours) to the contaminated dialysate, had a serum Al concentration of 50 μg/L (normal <60 μg/L). The serum Al concentration of another patient was 16 μg/L several weeks later. She also had a short exposure time to the contaminated dialysate because she went to Holland on June 3, 1996, shortly after installation and flushing of the new water pipe. The serum Al concentrations in three healthy controls were all below 10 μg/L (**Methods** section).

Subgroup analysis

The patients who survived the dialysis with contaminated dialysate were significantly younger than those who died (Table 1). The average body weight in the nonsurvivors was almost 30 kg below that of the survivors. Serum albumin was slightly but significantly lower in the nonsurvivors. The proportion of patients suffering from diabetes mellitus tended to be greater in the nonsurvivors than in the survivors (60 vs. 16%, $P = 0.11$), as was the proportion being anuric (80 vs. 47%, $P = 0.12$). It is noteworthy that the duration of exposure to the contaminated dialysate was even somewhat longer in the group of survivors. This was because two of the nonsurvivors (patients 1 and 6) were admitted to the hospital relatively early and consequently had a shorter exposure time. Survivors tended to have higher serum PTH concentrations (survivors, 308 ± 84 pg/mL; nonsurvivors, 125 ± 55 pg/mL, normal, 11 to 62 pg/mL).

DISCUSSION

We report a unique set of circumstances leading to a probable hard water syndrome followed by an epidemic of acute Al encephalopathy in a dialysis unit (Diatel) on the island of Curaçao. Traditionally, municipal water had been used without extended purification for the production of dialysate because the distributed distilled seawater was very pure and its ionic content low. Because of complaints of low water pressure in the dialysis center, the water distribution company replaced an old iron water distribution pipe by a new cement-coated pipe. Three of the predominant crystalline phases of the cement matrix are tricalcium silicate (nominally Ca_3SiO_5), dicalcium silicate (nominally Ca_2SiO_4), and tricalcium aluminate ($Ca_3Al_2O_6$). Possible dissolution reactions may be represented by $Ca_3SiO_5 + 5H_2O \leftrightarrow 3Ca^{2+} + H_4SiO_4^{\cdot} + 6OH^-$, $Ca_2SiO_4 + 4H_2O \leftrightarrow 2Ca^{2+} + H_4SiO_4^{\cdot} + 4OH^-$, and $Ca_3Al_2O_6 + 6H_2O \leftrightarrow 3Ca^{2+} + 2Al^{3+} + 12OH^-$ [9]. The purity of the water with a relatively low Ca concentration enhanced the leaching of Ca and Al from the cement coating into the water used to prepare dialysate.

Approximately four weeks after the new water distribution pipe had been put into use, a tentative diagnosis of a "hard water syndrome" was made. This syndrome is characterized by dialysis-related nausea and vomiting, weakness, and lethargy and is caused by hypercalcemia caused by elevated Ca concentrations in the dialysate [10]. Leaching of Ca from the new pipe was suspected, and the patients were transferred to a hospital dialysis unit using water softening and RO for water preparation and a low-Ca dialysate. This effectively ended exposure to the contaminated dialysate; the symptomatic patients improved, and the hypercalcemia disappeared. In retrospect, the Al intoxication may have contributed to the development of hypercalcemia because Al can decrease the incorporation of Ca into the bone by inhibiting bone formation [11]. Additional Ca from the dialysis fluid and therapy with vitamin D and Ca added to the severity of the hypercalcemia.

Unexpectedly, with a delay of days to weeks after ending exposure to the dialysate supposed to be contaminated only with Ca, 10 patients developed severe and progressive neurological symptoms and all died. Because all serum Ca levels already normalized, it became obvious that another contaminant had to be responsible for the delayed neurotoxicity. A lag time causing "acute" Al neurotoxicity has been observed in animal studies [12], as it seems likely that several steps are necessary in the process leading to Al encephalopathy and that

each step causes a delay in time before symptoms can occur [13]. The actual diagnosis of Al intoxication was later confirmed by very toxic serum Al concentrations and elevated brain Al levels that were four to eight times higher than normal. Acute Al intoxication is characterized by a neurological syndrome, including seizures, myoclonus, obtundation, and coma. Bone disease and dialysis dementia, features of classic chronic Al toxicity, are usually absent [14], but microcytic anemia can occur [8]. Sporadic cases have been reported after intake of Al-containing phosphate binders alone [15] and in combination with citrate-containing drugs [16], during treatment with desferrioxamine for chronic Al overload [17] and following intravesical Al infusion for hemorrhagic cystitis in renal patients [18]. Epidemic forms of acute Al intoxication have been described following the use of water for dialysis, which was severely contaminated with Al [8, 19].

In our center, the contamination of water used to prepare dialysate was caused by installation of a new cast iron water distribution pipe supplying water to the dialysis facility. Water distribution pipes are commonly coated on the inside with cement mortar to protect them from corrosion by the electrochemical action of water. These coatings can adversely affect the water quality because its constituents may leach from the cement matrix into the water increasing both its Ca content and pH [20]. Unfortunately, it was unknown to the local water distribution company and to the water industry in general that not only Ca, but also Al can leach from these cement mortars and cause excessively high water Al concentrations. Conditions that enhance Al leaching include low water alkalinity and hardness, relatively high water temperatures, and low or intermittent water flow. Unfortunately, all of these factors coincided in the situation, especially because Diatel was located at the dead end of a water main, resulting in the highest Al concentrations on the island. The pipe was partially bypassed by the water company (from 2200 to 1000 meters), but the Al leaching continued for at least two years [21]. Kidney patients with chronic renal failure—not on dialysis—living in the small distribution area were told not to consume the water because of the risk for developing Al intoxication. Elsewhere on Curaçao, where the same pipe was used, higher water flow conditions prevented Al concentrations to increase to very high levels.

In a number of European countries (for example, Germany, Denmark, and some parts of France), the authorities require that drinking water should be calcifying because of the pronounced effect on the corrosion of cement-mortar linings. This regulation is intended to protect cement materials and to reduce water quality deterioration, especially with regard to metal release [22]. If the water on Curaçao had been pretreated by the water company according to these regulations, Al leaching from the cement coating would probably have been less. Nevertheless, a crucial factor in the tragedy seems to be the deviant cement composition of the water distribution pipe with an Al content that was four times higher than usual [21], because Al leaching was not shown in similar circumstances and the use of different cement pipes. After the tragedy in Diatel, a study was performed in Holland to see whether the same problem existed there as well. Samples were taken on 20 locations with (standard) cemented pipes and asbestos cement pipes. Locations with "worst case scenarios" favoring the leaching of Al were chosen, defined as low flow, soft water, new pipes, and small diameter. The Al levels in the tap water in Holland never reached levels above 11 μg/L at any location [23], while the Al level in our case was 690 μg/L two months after the installation of the pipe. Cement linings with a high Al content are therefore probably inappropriate to distribute drinking water.

Although all patients were exposed to the contaminated dialysate for a similar period of time, 17 patients survived the Al intoxication with only minor symptoms, whereas 10 patients died from severe neurotoxicity. The nonsurvivors were the older population with a low body weight and lower serum albumin concentrations and a greater proportion of them had diabetes mellitus. This suggests that the general state of health was an important determinant of the chance of survival. In a review of 15 studies in animals and humans, an extremely narrow margin of safety between normal and toxic levels of Al in brain tissue seems to exists, with greater susceptibility in the older population [24]. More importantly, however, the serum Al concentrations were considerably higher in the nonsurvivors. This suggests that a similar Al load also caused higher Al concentrations at the tissue level in the low body weight patients, possibly because they had smaller distribution volumes. In addition, anuria was more common in the nonsurvivors, which is relevant because the main natural route of Al removal from the body is via the kidneys, and residual renal function protects against Al toxicity [25].

Although this is the first report of intoxication in dialysis patients caused by a water distribution pipe, it is not the first account of an intoxication linked to the water industry. In a recent and equally treacherous acute Al intoxication reported from Portugal, large amounts of Al sulfate had been used as a flocculating agent in the process of manufacturing drinking water. This was necessary because the concentration of suspended particles was excessive due to a long period of drought in the area. This severely contaminated water caused RO membrane fouling over several months of time, which might have decreased the ability to reject Al to as low as 30 to 50%, but in addition, the RO membranes were also temporarily bypassed several times for filter exchange and RO maintenance [26]. This resulted in an acute Al intoxication,

causing the death of 25 of 71 dialysis patients [8, 26, 27]. Both the intoxications on Curaçao and in Portugal underscore that dialysis centers should establish a good working relationship with the local drinking water production and distribution companies, as this may increase their awareness of the specific needs and problems of the dialysis community.

The catastrophe on Curaçao clearly demonstrates that physicians in charge of a dialysis unit cannot rely on the quality of the water produced by the water plant, no matter how excellent the specifications may be in terms of appropriateness for hemodialysis when water leaves the plant. The hard lesson was learned that the composition of the water could change unexpectedly and erratically in the water distribution system, making it absolutely unsuitable for preparation of dialysate upon its arrival in the dialysis unit without further water treatment. Therefore, dialysis centers should use extended purification procedures, including RO, at all times. In this respect, it is of note that dialysis without water preparation by RO was common practice until recently [28]. Nephrologists, who are responsible for the dialysate quality, often lack formal training in water safety and purification procedures. They therefore tend to rely unconditionally on the municipal water supply and the water purification system in their unit. That this is not always justified has been shown by several recent serious accidents with Al [8, 19], chloramine [29], fluoride [30], copper [31], hydrogen peroxide [32], sodium azide [33], and microcystins [34].

In summary, our sad experience shows that the use of extended water purification systems is imperative in hemodialysis. Furthermore, our experience and that of others indicate that continuous monitoring of the water before and after water treatment seems necessary as well and that dialysis centers should establish a good working relationship with local water production and distribution authorities. Finally, water purification procedures and water quality control perhaps deserve more attention in the training of nephrologists.

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